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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/691,528	10/24/2003	Olaf Wilhelm	2923-576	7396

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EXAMINER	
FEDOWITZ, MATTHEW L	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/691,528	WILHELM ET AL.	
	Examiner	Art Unit	
	Matthew L. Fedowitz	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

Applicant's arguments filed on March 16, 2005 have been fully considered but they are not persuasive.

Claims 1-17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over the PENTAPHARM Product Catalog, Xing *et al.*, DeVita *et al.* and Medenica *et al.* Part A of the rejection was directed to method claims 1-9, 16 and 17 and Part B of the rejection was directed to the composition and kit.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

More specifically, the applicant argues that the Pentapharm Product Catalog only discloses the L enantiomer of Nα(2,4,6-Triisopropyl-phenylsulfonyl)-3-amidino-(L)-phenylalanine-4-ethoxycarbonyl-piperazide and does not disclose the racemate or D-enantiomers. This argument is unpersuasive because the applicant specifically claims the L enantiomer of the compound above in claims 1, 10 and 16.

The applicant also argues that the Pentapharm Product catalog disclosure is only directed chemical products for research. This argument is unpersuasive because the application stated for the compound known as Nα(2,4,6-Triisopropyl-phenylsulfonyl)-3-amidino-(L)-phenylalanine-4-ethoxycarbonyl-piperazide is "a low molecular weight synthetic inhibitor of urokinase (uPA)" (see p. 23). The phrase "synthetic inhibitor of urokinase" is a pharmacologic classification rather

than a research chemical research classification. Therefore, the Pentapharm Product Catalog inherently suggests the use of the compound in pharmacologic applications and not chemical product analysis and purification. Furthermore, regardless of where the compound is listed in the catalog, it is pharmacologically classified and one skilled in the art would recognize the compound as having pharmacologic applications.

The applicant further argues that the Xing et al. reference is narrowly directed to the urokinase inhibitor B-428; however, the reference broadly states that "the role of cell-associated uPA and its cell surface receptor (uPAR) in extracellular matrix degradation, cellular invasiveness and tumor progression is well documented" and that "inhibition of uPA activity and interruption of uPA/uPAR interaction is, therefore, and attractive target for blocking the cellular invasiveness of cancer" (see p. 3590 first column). Therefore, the applicant's argument is unpersuasive because Xing et al. directs one skilled in the art broadly to the use of urokinase inhibitors.

The applicant then argues that Tamoxifen is not a cytotoxic agent. The definition of "cytotoxic" is that which causes cellular injury or death. The applicant only directs their argument to compounds, which cause cell death, and does not fully realize that cytotoxicity encompasses a range from cellular injury to cellular death. Furthermore, one skilled in the art would realize that numerous studies exist that are directed to the cytotoxicity of Tamoxifen. Furthermore, the applicant then states that Tamoxifen is only used for tumors that contain estrogen receptors; however, only a novice in the art would make this statement because one skilled in the art would know that there are numerous studies that are directed to combination

chemotherapy for estrogen receptor negative tumors. Therefore, the applicant's arguments are found to be unpersuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, the motivation to combine the references for the method claims is provided by Xing *et al.* by the statement that "because the uPA/uPAR system plays a key role in tumor invasion and metastasis, inhibition of cell surface uPA activity is an attractive therapeutic target for controlling cellular invasiveness in cancer (see page 3585 second column second full paragraph). And the motivation to combine the references for the composition and kit claims is found in Xing *et al.* where it states that "the efficacy of currently available therapies for breast cancer is restricted by the disseminated nature of the disease, which is characterized by the progression of the majority of tumors to a phenotype that is resistant to both cytotoxic and hormonal therapies" and "therefore, the development of a complementary approach ... is required" and that "inhibition of uPA activity and interruption of uPA/uPAR interaction is, therefore, an attractive target for blocking cellular invasiveness of cancer" (see pp. 3589-3590 first paragraph of discussion).

Therefore, all of the applicant's arguments are found to be unpersuasive and all of the rejections are maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew L. Fedowitz whose telephone number is (571) 272-. If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, James O. Wilson, can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Matthew L. Fedowitz, Pharm.D., Esq.

James O. Wilson , Supervisory Patent Examiner
Art Unit 1623